

ABSTRACT OF THE DISCLOSURE

Methods are provided for the *in vivo* introduction of an expression cassette into a target cell of a vascularized organism, e.g., a mammal, in manner such that the encoded protein of the introduced expression cassette is persistently expressed at a high level in the target cell. In the subject methods, an aqueous formulation of a minimal plasmid vector that includes the expression cassette is administered into the vascular system of the organism. The minimal plasmid vector employed in the subject methods is one that provides for persistent and high level expression of an expression cassette that is present on the vector in a manner that is substantially expression cassette sequence and direction independent Also provided are the minimal plasmid vectors employed in the subject methods. The subject methods and compositions find use in a variety of different applications, including both research and therapeutic applications, and are particularly suited for use in the *in vivo* delivery of nucleic acids encoding protein products, particularly where persistent, high level protein expression is desired without integration of the vector into the host genome.

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